Horizontal transfer of antiviral defences between bacterial species

Supervisory team:
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Project description:
The discovery of CRISPR-Cas has arguably been one of the most influential discoveries in biology of the past decades. CRISPR-Cas systems that are encoded on bacterial genomes to protect against viral and plasmid infections. This has been utilised to safeguard industrial fermentations, and recently been exploited to eradicate antimicrobial resistance plasmids from microbial communities under laboratory conditions. Furthermore, the recent development of CRISPR-Cas genome editing is facilitating ground-breaking strategies in science, agriculture, medicine and pest management, such as synthetic gene drives to eradicate disease vectors. These examples highlight some of the most significant economic and health impacts that CRISPR-Cas-based technologies are already generating, and further technological advances continue to be developed at a rapid pace.

Many of these applications require that the genes encoding CRISPR-Cas are stably expressed across many generations. Yet, long-term studies that examine genetic and transcriptomic stability of these systems are lacking. Understanding how regulatory networks evolve to facilitate the regulation of novel gene functions will ultimately develop our understanding of fundamental processes, such as how genetic innovations evolve, as well as helping to explain the natural diversity we see in CRISPR-Cas regulatory mechanisms. This project will use a combination of experimental evolution, molecular genetics, synthetic biology and network modelling to understand how CRISPR-Cas transcriptional regulation evolves. Based on classical evolutionary theory, we hypothesise that we can predictably manipulate the way CRISPR-Cas gene regulation evolves in bacteria following the synthetic or natural transfer of CRISPR-Cas genes to a naïve bacterial host. An ability to predictably evolve CRISPR-Cas gene regulation would be truly ground-breaking, and would have clear implications for the use of these systems in industry and in the development of strategies for eradicating antimicrobial resistance. The project will benefit from expertise in evolution of novel regulatory and genetic innovations (Taylor, Bath), P. aeruginosa CRISPR-Cas evolution (Westra, Exeter), P. fluorescence-phage coevolution (Buckling, Exeter) and regulatory network modelling (Rogers, Bath). Throughout this interdisciplinary project, the student will receive extensive training in experimental evolution, molecular microbiology, genetics and modelling. The student will be based in the Taylor lab as part of the Milner Centre for Evolution at the University of Bath (currently 3 PhD students) with opportunities to work in the Westra and Buckling labs at the Environment and Sustainability Institute at the Cornwall campus of the University of Exeter, and with the Roger lab in the Department of Maths at the University of Bath.